

A Report from the Russian Front in the Global Fight against Drug-Resistant Tuberculosis

Can the campaign against MDR-TB in Russia help curb the global epidemic?

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ON THE MEND: Misha K. has suffered from two bouts of tuberculosis, the second of which proved to be the hard-to-treat, multidrug resistant variety of the disease.

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TOMSK, RUSSIA—Misha K.—ex-con, ex-drug abuser, family man—arrived promptly at 4 P.M. for his daily dose of antibiotics. He is fighting his second bout with tuberculosis (TB), both times caught while serving a four-year prison term in this small city at the edge of Siberia. His crime: petty thievery to support his drug habit.

The first time, prison doctors put him on a nine-month regimen of antibiotics, a standard prescription for routine cases of so-called susceptible TB. The susceptibility label is something of a misnomer. When streptomycin was discovered in the 1940s, the miracle drug was hailed as the magic bullet that cured TB. But the wily *Mycobacterium tuberculosis*

quickly developed resistance. Now it takes four drugs to cure "susceptible" TB.

The four-drug regimen worked for Misha. But shortly before his release, he caught TB a second time, probably from another prisoner. Again he was put on standard four-drug therapy. But when he got out, he stopped taking the pills. "The first time it took nearly a

year," said Misha, who did not want his last name used. "So by the second time I was on the drugs, I became very tired of it all."

It was not an irrational response. The initial few months of standard therapy succeeds in knocking out most of the bacteria, and the symptoms disappear. But some *M. tuberculosis* develop a waxy coat and hide in the recesses of the lung. Among those survivors are mutant strains, unfazed by some of the drugs. When the four-drug cocktail is removed prematurely, these strains become dominant, and the bacteria cells multiply at *M. tuberculosis*'s slow but inexorable once-a-day rate.

A year after leaving prison, Misha's disease came roaring back—this time multidrug resistant, or MDR-TB. Tired, coughing blood, the 30-year-old factory worker was told by civilian health authorities that he now had to take six drugs a day, including one by injection, or he would probably die. DOTS (short for "directly observed therapy, short course"—the World Health Organization's prescription for proper treatment of susceptible TB) gave way to DOTS-Plus, the psyche-bending two-year regimen of six drugs that it takes to defeat MDR-TB.

This past June, when I interviewed Misha at the dispensary that coordinates TB care in the region, he was well into his second year of treatment. "He's almost cured," said an upbeat Guzel Davidova, the nurse who prepares and observes his daily treatment. "I'm trying to make a new life now," whispered the rail-thin father of two. As he absently fingered his right forearm's deep purple scar, a souvenir from his prison days, he looked up and added, "I'm off drugs completely." He wasn't referring to the TB drugs, not yet anyway.

The Siberian provinces of the central Russian plateau—poor, even by Russian standards, with high rates of alcoholism, drug abuse and a large prison population—are among the epicenters of a worldwide epidemic of drug-resistant tuberculosis. Whereas the 490,000 reported cases of MDR-TB account for just a small fraction of the 9.2 million new cases and 1.7 million deaths from TB reported to the World Health Organization in 2006, MDR-TB represents a significant global public health hazard. In parts of Siberia, it accounts for more than 15 percent of all cases.

Left untreated, the resistant TB can spread to the general population through the usual route: airborne transmission of spewed sputum. Treated poorly, it can spawn extensively drug-resistant TB (XDR-TB), a more virulent and nearly impossible-to-treat version of the disease.

And the Western world, which three decades ago believed it had conquered the disease, is hardly immune from these aggressive new versions of it in a globalized economy. Atlanta lawyer Andrew Speaker generated a national uproar last year after gallivanting around the world with a resistant strain of TB that he might have picked up while doing charity work in Vietnam, but even more troubling cases involve itinerant immigrants like Robert Daniels, who probably contracted MDR-TB while serving time in a Russian prison for marijuana possession.

Daniels told National Public Radio that he stopped taking TB drugs because he was "feeling fine." After leaving a wife and small son behind in Moscow, he wound up in a Phoenix hospital under quarantine with XDR-TB. So far, only 1 percent of the 13,148 TB cases reported in the U.S. in 2006 involved drug-resistant strains.

"We're all connected by the air we breathe," says Thomas Frieden, New York City's health commissioner who won plaudits for successfully combating an MDR-TB outbreak in the city's jails in the 1990s. "MDR-TB is a serious problem. It can spread explosively. But it's a symptom of a larger problem—that we're not treating susceptible TB well even though we have the tools to make tremendous progress."

In Tomsk, the tools he's talking about—drug treatments and a comprehensive model for delivering them—are finally being deployed, although only after a concerted campaign over more than a decade by global health authorities, along with nonprofit, nongovernmental organizations (NGOs) including Boston-based Partners in Health (PIH). These groups have marshaled international aid to help rebuild the local prison and the public health infrastructure for combating TB, which had nearly collapsed after the fall of Soviet communism in 1989.

The program's architects claim that by getting the local authorities to focus on treating MDR-TB, they have also reinvigorated the community's response to susceptible TB. It is a model that is now being taught to TB physicians throughout the Commonwealth of Independent States (CIS), an organization made up of Russia and some of the other former republics that comprised the Soviet Union, and one that is exportable to other countries, the advocates say. They believe it could help the world public health community meet the goal established in 2006 of halving TB's global prevalence and mortality by 2015.

The reality is that the overall rates of TB here have only recently begun to drop, and the country as a whole remains far behind meeting the 2015 goals. "The problem in Russia is only growing," says Michael Kimerling of the Gorgas Tuberculosis Initiative at the University of Alabama at Birmingham, who helped kick off the TB-treatment push here in the late 1990s and this month takes over managing the Bill and Melinda Gates Foundation program for treating TB around the world. "There's been a lot of money spent but it is really every bit the problem it was 10 years ago."

This In-Depth Report will explore these efforts to combat TB: at a hospital that has dramatically lowered the reinfection rate in Tomsk's prison; in civilian hospitals and rural settings that have gone from ignoring MDR-TB cases to successfully treating them—even though a single patient's drugs can cost several thousands of dollars a year; and through a door-to-door campaign that delivers DOTS to hard-to-reach cases in their own homes. A final article will look at the new diagnostic tools and drugs in development that could simplify treatment of the disease.

What little progress there is here hasn't come easy. Promoters of the program had to overcome initial skepticism by a Russian TB establishment, which has a long, proud and

idiosyncratic approach to treating the disease. Even now, Russia's top TB doctor, the octogenarian surgeon Mikhail I. Perelman, scoffs at the notion that the Tomsk model and NGOs' contributions will lead to dramatic changes. "DOTS—this system was developed for the poorest countries of Africa. These places are not like Russia," he says.

But TB thrives anywhere there are high levels of unemployment, poverty, alcoholism, drug abuse or co-infections like HIV—conditions that know no borders. And when people are living in close quarters under chronic stress and with poor nutrition—such as existed in Russia's prisons in the 1990s—the danger of an outbreak is ever present.